The Glycoproteinoses: Second International Workshop on Advances in Pathogenesis and Therapy

The second international workshop on glycoprotein storage diseases brought together nearly two dozen scientists and a hundred professional and family delegates from eight countries for an intensive two-day scientific workshop followed by an additional day of a family conference sponsored by the ISMRD. The scientific meeting began with a plenary lecture by Dr. Elizabeth Neufeld on the history and most recent breakthroughs in the area of enzyme replacement therapy (ERT) for the glycoproteinoses and related lysosomal diseases. This was followed by sessions focused on progress in development and utilization of animal models, delineation of pathogenic mechanisms and advances in therapy for mannosidosis and fucosidosis. Included here were reports of research progress in ERT, intrathecal ERT, and gene therapy for murine, guinea pig and cat models of α-mannosidosis by Drs. J. Blanz, J. Hopwood, J. Wolfe, and C. Vite, and a canine model of fucosidosis by Dr. R. Taylor. While it was noted that no mouse model of fucosidosis has yet been developed (a shortcoming also noted at the first glycoproteinosis workshop in 2002), Dr. K. Friderici described the development of a murine knockout model of β-mannosidosis. A special lecture on the discovery of I-cell disease and related developments was given by Dr. J. Leroy, followed by presentations on murine models of sialidosis and galactosialidosis by Dr. A. d’Azzo, the I-cell disease model in cats by Dr. M. Haskins, and mucolipidosis (ML) II in zebra fish by Dr. R. Steet. Drs. T. Braulke and S. Tiede presented new findings on the molecular analysis of MLII and MLIII diseases. The second day of the workshop focused to a greater degree on human clinical conditions, including the importance of natural history studies by Drs. Patterson, Whitely and Cathey. The European activities directed at α-mannosidosis (the HUE-MAN Consortium) were described by Drs. C. Friis and M. Beck. Progress in the use of umbilical cord transplantation and bone marrow transplantation in humans was summarized by Drs. J. Kurtzberg and C. Peters, respectively, and the use of ERT in MLII/III patients was described by Dr. M. Vellard. Summaries of presentations on pathophysiological issues were provided by Dr. S. Walkley, on therapy issues by Dr. M. Patterson, and an overall wrap-up of the workshop by Dr. E. Neufeld. A major outcome of the meeting was a broad discussion on the need to revisit the nosology of MLII/MLIII diseases as a result of advances in the molecular etiology of these conditions described at this meeting. A group of six participants (Drs. Cathey, Tiede, Beck, Leroy, and Neufeld) pledged to follow-up with a written summary of the suggested changes, and this report has recently been published. Briefly, MLII (I-Cell disease) and MLIIIa (Pseudo-Hurler Polydystrophy) diseases have been re-designated as MLII alpha/beta and MLIII alpha/beta, respectively. While clinically distinct, both are caused by defects with the alpha or beta subunits of the UDP-GlcNAc 1-phosphotransferase (GlcNAc-PT) enzyme which are encoded by the same gene. MLIIIC disease, also known as the MLIII variant, has been designated MLIII gamma, since this disease, while showing some clinical similarity to cases of MLIII caused by defects in alpha/beta subunits, results specifically from defects in a separate gene encoding the gamma subunit of GlcNAc-PT.

At the close of the meeting there was the consensus view offered that this second international workshop fulfilled its goal to bring together scientists and clinicians from around the world to synergize research and therapy efforts for the glycoproteinoses.

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